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Producers of Quality Nonprescription Medicines and Dietary Supplements for Self Care

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Nonprescription Drug Manufacturers Association

April 26, 1999

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, MD 20852

Re: Docket No. 99N-0386. Talking with Stakeholders about FDA Modernization: Notice of Meetings and Teleconference. Federal Register 64: 13804-13806, 1999.

Dear Madam or Sir:

These comments are submitted by the Consumer Healthcare Products Association (CHPA) to the Food and Drug Administration (FDA) in response to FDA's announcement of a live satellite teleconference and meetings in eight major cities across the country as a means for the agency to answer questions from viewers and listen to suggestions about how FDA can better carry out its mandates.

CHPA, formerly known as the Nonprescription Drug Manufacturers Association (NDMA), is the 118-year-old trade organization representing the manufacturers and distributors of national and store brand dietary supplements and nonprescription medicines. CHPA's membership includes over 200 companies involved in the manufacture and distribution of these self-care products and their affiliated services (e.g., raw material suppliers, research testing companies, contract manufacturing companies, advertising agencies, etc.).

FDA asks five questions for specific comment by stakeholders taking part in the teleconference and meetings. CHPA supports the dialogue in each of these areas, but

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focuses in these written comments on three questions relating to science-based decisions. Specifically FDA asks:

1. "What actions do you propose the Agency take to expand FDA's capability to incorporate state-of-the-art science into its risk-based decision-making?"

2. "What actions do you propose to enable FDA and its product centers to focus resources on areas of greatest risk to the public health?"

3. "What additional actions do you propose for enhancing communication processes that allow for ongoing feedback and/or evaluation of our modernization efforts?"

Our comments request specific actions under sections I.A. and III, below, relating to needed refinements on CDER's [1] handling of Rx-to-OTC switch decisions and CFSAN's[2] development of a MaPP on meetings with external constituencies. We also urge continued support by the agency on joint educational efforts in the compliance area, and support CFSAN's program priority for developing an overall strategy on dietary supplements. Section IV provides a list of our requested actions.

I. FDA Question: What actions do you propose the Agency take to expand FDA's capability to incorporate state-of-the-art science into its risk-based decision-making?"

CHPA has two separate comments in answer to the question of expanding FDA's capability to incorporate state-of-the-art science into its risk-based decision-making. The first relates to Rx-to-OTC switch and FDA's recent action that questions the basic approach FDA is taking to benefit/risk-based decision-making relating to OTC

[1] CDER: Center for Drug Evaluation and Research.
[2] CFSAN: Center for Food Safety and Applied Nutrition.

availability. The second relates to CHPA's continued support for industry-agency partnerships relating to joint educational efforts on technical aspects of good manufacturing practices in order to ensure a mutual understanding of, and commitment to, the best applied technology in Good Manufacturing Practices.

A. Rx-to-OTC Switch

In its March 1999 "A Message to FDA Stakeholders: FDA's Progress in Implementing FDAMA," FDA states:

> "Science-based decisions are made throughout the life span of products from initial research, development and testing, through production, marketing and consumption. These decisions require the best science to identify, evaluate and balance product risks and benefits. It is crucial that FDA's staff in collaboration with product sponsors develop a shared understanding of new science and technologies and their effect throughout a product's life span. What actions do you propose the Agency take to expand FDA's capability to incorporate state-of-the-art science into its risk-based decision-making?"

In the same document, FDA states that "Dr. Henney places a high premium and priority on making sure that science anchors FDA's decision-making processes and critical policy decisions. CHPA strongly supports this public health objective, particularly as it applies to the reclassification of prescription products to nonprescription status (i.e., Rx-to-OTC switch).

CHPA proposes[3] that FDA establish a CDER policy that would require the agency to fully explain its positive and negative switch decisions and in the process to reconsider its Guidance for Industry on the "OTC Treatment of Hypercholesterolemia"

and thereby further ensure that a data-driven process is used throughout the agency to permit selected prescription drugs, including cholesterol-lowering drugs, to be available OTC in the future. Such a policy would articulate the long-standing approach that FDA has used for most, if not all, Rx-to-OTC switch decisions – a case-by-case, weight-of-the-evidence, data-driven, dialogue-driven approach.

The public health history of Rx-to-OTC switch has been exemplary. Since 1972 at the beginning of the OTC Review and through the subsequent further development of the OTC NDA process of drug approval, over 78 ingredients, dosage forms, dosages and indications have been switched from Rx-to-OTC status (see Attachment). With the exception of metaproterenol, which was switched and then switched back to Rx status in 1983 largely on the basis of medical opinion vs. data [4], Rx-to-OTC switch ingredients have had a remarkable success story, providing significant cost savings to the public health system[5] and important self-care therapeutics for the consumer (e.g., fluoride, vaginal antifungals, nicotine-replacement therapy, cromolyn sodium for prevention of allergy symptoms, among many others).

Importantly, under the Durham Humphrey Amendments to the FD&C Act, any drug which cannot be safely used without medical supervision must be labeled for sale and be dispensed only by prescription of a licensed practitioner; otherwise it is OTC. Hence, by law and regulation in the United States, drugs are prescription by exception.

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[3] See also comments from CHPA (formerly NDMA) to FDA Docket No. 98N-0044: Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body. *Federal Register* 63: 23624-32, April 29, 1998.

[4] "Despite the advisory committee's vote, FDA continues to believe that a careful weighing of risks and benefits supports the proposal that metaproterenol sulfate metered-dose inhaler should be made available to asthma sufferers without a prescription. Metaproterenol sulfate is a safe and effective drug, and nothing in the criticisms submitted to FDA or voiced at the advisory committee meeting is inconsistent with that judgment. ... Nevertheless, FDA cannot fail to respect the judgment of specialists in the field who believe that OTC availability of metaproterenol sulfate metered-dose inhaler poses a health risk. These practitioners have made clear that they have important reservations about FDA's decision to propose that metaproterenol sulfate be marketed OTC." Proposed Rule and Related Notice re Over-the-Counter Marketing Status of Metaproterenol Sulfate Metered-Dose Inhaler Drugs For Use as a Bronchodilator [48 F.R. 24925-28 (6/3/83)].

[5] Kline & Company, Inc.; Economic benefits of self medication. A final report to NDMA, May 15, 1997 - on file at CHPA.

In other words, "If it can be OTC, it must be OTC." The law, however, does not state the approach that FDA should take in determining why a drug cannot be safely used without medical supervision. However, the applied approach by CDER has been for most, if not all, Rx-to-OTC switch decisions a case-by-case, weight-of-the-evidence, data-driven and dialogue-driven process to determine OTC availability. This approach is entirely consistent with the legal mandate that, if a product can be OTC, it must be OTC.

Because FDA has demanded an ever-increasing data base to support more complicated switch decisions, the proposition that a product or condition can be switched to OTC or self-care status can be regarded a testable hypothesis. Mutual recognition of this concept by CDER and industry is vital if Rx-to-OTC switch is to be a viable approach for future OTC product introductions.

In other words, OTC availability is usually distilled to a basic question (or questions) that, if tested, would contribute meaningfully to OTC benefit/risk decisions pertaining to OTC availability. For example, drugs may show relatively modest improvements in symptoms over placebo in controlled trials, and the potential OTC safety concerns for an Rx parent of the switch candidate are relatively well characterized through its Rx marketing experience (e.g., potential drug-drug interactions, development of viral resistance, masking of more serious conditions, etc.). Thus, the testable switch hypothesis might be: Does the OTC availability of candidate "X" result in an unreasonable level of excess cases going undiagnosed? We have the available tool to test (i.e., disprove) this hypothesis – the actual use study, wherein OTC usage in a simulated OTC environment can be compared to that in a simulated Rx environment. Other questions, perhaps relating to effectiveness, might also have to be tested and added to a distilled benefit/risk question, such as: Is a modest (x%) improvement in one or more specific clinical endpoints related to self-care of the condition or disease under study worth the unlikely (but perhaps uncertain) risk of a particular side effect (e.g., GI side effects, drug-drug interaction, etc.) or consequence (e.g., unacceptable level of undiagnosed cases, or viral resistance, etc.)?

With this approach, the need for a health professional as a learned intermediary in the use of any drug for a potential or actual OTC condition is a testable hypothesis. Scientific and clinical data - not medical opinion alone - are the drivers for expanding the OTC paradigm with novel Rx-to-OTC switches.

However, on October 21, 1997, FDA issued a Guidance for Industry on the "OTC Treatment of Hypercholesterolemia" that stated:

> "It is CDER's view that (a) health care practitioner supervision in the diagnosis and ongoing management of hypercholesterolemia is essential for safe and effective use of drug products to treat this condition and (b) this supervision is assured within the context of prescription access to the appropriate drug(s) for the individual patient. CDER therefore believes that drugs for the treatment of hypercholesterolemia should not be sold OTC in the United States."

This decision was made after review by an FDA advisory committee of a comprehensive, well-designed, well-conducted actual use study that showed a remarkable set of study results supporting the safety and effectiveness of Questran for OTC use, as well as an equally remarkable level of interest by the American public in having widely available cholesterol-lowering agents.

This decision and subsequent "guidance" on OTC hypercholesterolemic agents comes at a time when the agency is grappling with claims for dietary supplements, specifically statements of nutritional support (or structure/function claims). While the Association has stated its firm support for the provisions of the Dietary Supplement and Health Education Act (DSHEA) in comments to the agency on these types of dietary supplement claims (see footnote 3) and has urged an alternate proposal to their

regulation, CPHA's comments and FDA's proposal share the basic concept of permitting dietary supplements to make claims relating to cholesterol levels.

Further, prescription drugs can make cholesterol claims, as can foods as well as dietary supplements. OTC drugs cannot. CHPA urges FDA to consider the incongruity of this situation. An OTC drug for lowering cholesterol levels would be labeled with ample information approved by FDA, fit the OTC paradigm that in selected cases requires a physician visit prior to use (e.g., as in the case of OTC antifungals for vaginal candidiasis), and be tested through appropriately designed label comprehension and actual use studies. A dietary supplement may make maintenance claims for cholesterol levels without FDA review. While CHPA supports such a claims structure for dietary supplements under DSHEA, the Association believes that to regulate sensibly, the agency must consider the bigger picture, taking account of the full range of products available for health care. Foods, dietary supplements, OTC drugs, and prescription drugs are all part of the self-care product continuum. All of them, except OTC drugs, currently may make, or would be able to make under FDA's structure/function proposal, cholesterol-related claims.

FDA's declaration in its Guidance document that OTC drugs do not fit in this continuum does not make sense from a public health policy standpoint, especially against the background of the Questran studies described above that supported a switch NDA. CHPA believes cholesterol-lowering drugs are appropriate for OTC use and would contribute significantly to consumer health and understanding of disease. CHPA urges FDA to rescind its Guidance for Industry on the "OTC Treatment of Hypercholesterolemia" and instead explain in detail the specific questions that would have to be answered by well-designed research before drugs for hypercholesterolemia can be made available without a prescription. Only in this way can the dialogue- and data-driven process that has characterized Rx-to-OTC switch over the last 25 years be preserved.

In enacting DSHEA, Congress recognized the need to maintain a balance between providing expanded self-care opportunities to consumers through dietary supplements on the one hand and preserving incentives for drug research and development on the other. FDA's decision on the switch of Questran and its Guidance for Industry on the "OTC Treatment of Hypercholesterolemia" declaring that such drugs should not be sold OTC in the United States is a frank disincentive to research and development in other potential switch areas, where dietary supplement products make structure/function claims in the same general category. Congress did not intend for FDA to chill drug research and development that could benefit consumers.

Therefore, in answer to FDA's question, "What actions do you propose the Agency take to expand FDA's capability to incorporate state-of-the-art science into its risk-based decision-making?", CHPA asks that FDA recapture its long-standing data-driven, dialogue-driven approach to Rx-to-OTC switch decisions by ensuring a CDER policy that would require the agency to fully explain its negative switch decisions, in order to identify limitations and omissions in the sponsoring company's submission. In this way, when confronted with a negative switch decision, a company has the opportunity to determine what further, if any, state-of-the-art research might be undertaken to support a re-proposal for OTC availability of a prescription drug active ingredient – consistent with the FDC Act that, if it can be OTC, it must be OTC and consistent with the premise that switch is essentially a testable hypothesis. FDA would thus be assured of having the best science to support its benefit-risk decisions about OTC availability of drug products. In the process of developing such a CDER policy, the negative guidance on OTC antihypercholesterolemics would be appropriately rescinded and presumably amended.

We look forward to the agency's response on this point.

B. Applied Technology and Good Manufacturing Practices

CHPA has had a long-standing partnership with the CDER Office of Compliance in terms of joint educational efforts, including CHPA's annual Manufacturing Controls Seminar (now in its 31st year), industry briefings, Small Business seminars, and regional meetings on specific issues identified as current manufacturing problem areas. These sessions have been invaluable. They have also shown an important approach to building the science base of the agency, through the collaboration of FDA with leading industry scientific/technical experts.

Our goal is to address current problem areas or evolving technological issues and create joint educational meetings with the agency in order to raise awareness about the identified issues, establish a higher level of understanding of the agency's expectations for current Good Manufacturing Practices, and share scientific advances in the production of quality drug products. Such jointly developed educational meetings allow the agency to make use of state-of-the-art scientific expertise already available in the industry.

These efforts have an important salutary effect on product quality. A notable example of the practical benefits of this joint educational approach was seen following the 1988 joint regional seminars on label mix-ups. The frequency of what had been the number one cause of product recalls dropped dramatically. We also understand that our programs and those of other associations are regarded by the Office of Compliance as important preventive compliance vehicles.

In sum, we ask FDA to continue its commitment to these types of partnerships with industry. Not only do such educational activities have a direct positive impact on product quality, thereby serving FDA's mission to protect the public health, they do so in a value-added way by saving agency resources, since industry assumes the administrative and financial burdens while providing input to FDA on the latest industry technology.

II. FDA Question: "What actions do you propose to enable FDA and its product centers to focus resources on areas of greatest risk to the public health?"

While CHPA does not believe that dietary supplements in general represent an area of greatest risk to the public health, the Association takes this opportunity to comment on a related area identified by CFSAN in its 1999 Program Priority document. Occasionally, certain ingredients, such as GBL, may be marketed as dietary supplements and FDA must take appropriate action to protect the public health. To do this consistently and coherently, FDA must have an overall strategy on dietary supplements, as suggested in CFSAN's Program Priority document. Our comments address this point.

In January, 1999, the Center for Food Safety and Applied Nutrition (CFSAN) published its 1999 Program Priorities document in which it stated as a Priority A activity its intention to "develop an overall strategy for achieving effective regulation of dietary supplements under the Dietary Supplement and Health Education Act (DSHEA)" by addressing "all elements of the dietary supplement program, including: boundaries between a dietary supplement and a conventional food, between a dietary supplement and a drug, and between a dietary supplement and a cosmetic product; claims; good manufacturing practices; adverse event reporting, review and follow-up; laboratory capability; research needs; enforcement; and resource needs." CFSAN also identified "stakeholder outreach" for both obtaining input to an overall strategy and effective communication. CHPA strongly supports a stakeholder outreach process to address these Priority A activities for CFSAN.

At the March 25, 1999, hearing of the Government Oversight Committee, both Dr. Henney and CFSAN's director, Mr. Joe Levitt, stated the agency's intent to develop this overall strategy in 1999. Given the effective operations of CFSAN in implementing the President's Food Safety Initiative, we are encouraged that the Priority A activity on dietary supplements might be undertaken by a similar administrative approach designed to define the agency's policy, operations and implementation plan through stakeholder

input. In this way, stakeholders can help define the needed priorities on dietary supplements, thereby allowing the agency to efficiently focus its resources. As FDA moves forward in this area, CHPA will provide specific detailed comments on FDA's overall strategy for dietary supplements.

III. FDA Question: "What additional actions do you propose for enhancing communication processes that allow for ongoing feedback and/or evaluation of our modernization efforts?"

Recent meetings between the Center for Food Safety and Applied Nutrition and CHPA have been excellent in content and form. Our response to this question is therefore not a criticism but rather a suggestion based on an association's view of the workings of two of the agency's main Centers – CFSAN and CDER.

Several years ago, CHPA worked with CDER in developing a MaPP for meetings by CDER with its external constituencies (MaPP 4512.1). This MaPP, which was subsequently updated with provisions from FDAMA, has been very successful in ensuring efficient meetings with defined agendas and questions, as well as subsequent action items. We encourage CFSAN to adopt a similar MaPP, as a proactive management step.

IV. Conclusion and Requested Actions

In conclusion, CHPA thanks FDA for the opportunity to provide the view of the consumer healthcare products industry. We look forward to feedback from the agency on our four areas of comment. We request that FDA:

- Develop of a CDER policy that would require the agency to fully explain its negative switch decisions in order to identify limitations and omissions in company submissions;

- In the course of developing such a guidance, rescind and presumably amend the negative guidance on OTC antihypercholesterolemic agents;
- Continue the agency's commitment to educational partnerships with industry;
- Engage, as planned, in a stakeholder outreach approach to developing an overall strategy on dietary supplements;
- Develop a "meetings MaPP" for CFSAN, similar to MaPP 4512.1 used by CDER.

Sincerely yours,

R. William Soller, Ph.D.

R. William Soller, Ph.D.
Senior Vice President
Director of Science and Technology

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Consumer Healthcare Products Association

Ingredients & Dosages Transferred From Rx-to-OTC Status (or New OTC Approvals) by the Food and Drug Administration Since 1975

April 16, 1999

	INGREDIENT	ADULT DOSAGE	PRODUCT CATEGORY	DATE OF OTC APPROVAL	PRODUCT EXAMPLES
1.	brompheniramine maleate	4 mg./4-6 hours (oral)	antihistamine	September 9, 1976	Dimetane (A.H. Robins)
2.	chlorpheniramine maleate	4 mg./4-6 hours (oral)	antihistamine	September 9, 1976	Allerest (Pharmacraft), Chlor-Trimeton (Schering), Contac (SmithKline), Sudafed Plus (Warner-Lambert)
3.	oxymetazoline hydrochloride	0.05% aqueous solution (topical)	nasal decongestant	September 9, 1976	Afrin (Schering), Duration (Plough), Dristan Long Lasting (Whitehall), Neo-Synephrine-12 Hour (Bayer)
4.	pseudoephedrine hydrochloride	60 mg./4 or 4-6 hours (oral) 240 mg. max./24 hours	nasal decongestant	September 9, 1976	Sudafed (Warner-Lambert), Neo-Synephrinol (Bayer)
5.	pseudoephedrine sulfate	60 mg./4 or 4-6 hours (oral)	nasal decongestant	September 9, 1976	Afrinol (Schering), Chlor-Trimeton (Schering)
6.	xylometazoline hydrochloride	.01% aqueous solution (topical)	nasal decongestant	September 9, 1976	Orrivin (Ciba)
7.	doxylamine succinate (NDA)	25 mg. single dose only (oral)	sleep-aid	October 18, 1978	Unisom (Pfizer)
8.	hydrocortisone	0.25 to 0.50% (topical)	antipruritic (anti-itch)	December 4, 1979 +	Cortaid (Upjohn), Lanacort (Combe)
9.	hydrocortisone acetate	0.25 to 0.50% (topical)	antipruritic (anti-itch)	December 4, 1979 +	Bactine (Miles), Caldecort (Pharmacraft)
10.	acidulated phosphate fluoride rinse	0.02% fluoride in aqueous solution	dental rinse	March 28, 1980	
11.	sodium fluoride rinse	0.05% aqueous solution (topical)	dental rinse	March 28, 1980	Fluorigard (Colgate-Palmolive)
12.	stannous fluoride gel	0.4% gel (topical)	anticaries gel	March 28, 1980	GelKam Gel (Colgate-Palmolive)
13.	stannous fluoride rinse	0.1% aqueous solution (topical)	dental rinse	March 28, 1980	Stan Care (Block)
14.	ephedrine sulfate	0.1 to 1.25% (topical)	anorectal/vasoconstrictor	May 27, 1980	Pazo Ointment (Bristol-Myers)
15.	epinephrine hydrochloride	0.005 to 0.01% (topical)	anorectal/vasoconstrictor	May 27, 1980	
16.	phenylephrine hydrochloride	0.25% (topical)	anorectal/vasoconstrictor	May 27, 1980	
17.	chlorpheniramine maleate (NDA)	12 mg./12 hours (oral timed-release)	antihistamine	July 23, 1981	Triaminic 12 (Sandoz)
18.	phenylpropanolamine hydrochloride (NDA)	75 mg./12 hours (oral timed-release)	nasal decongestant	July 23, 1981	Triaminic 12 (Sandoz)
19.	diphenhydramine hydrochloride (NDA)	25 mg./4 hours (oral)	antitussive	August 7, 1981	Benylin (Parke-Davis)
20.	haloprogin	1.0% (topical)	antifungal	March 23, 1982	
21.	miconazole nitrate	2.0% (topical)	antifungal	March 23, 1982	Micatin (Ortho)
22.	diphenhydramine hydrochloride	50 mg. single dose only (oral)	sleep-aid	April 23, 1982	Sominex 2 (Beecham), Sleep-eze 3 (Whitehall)
23.	diphenhydramine monocitrate	76 mg. single dose only (oral)	sleep-aid	April 23, 1982	Excedrin PM (Bristol-Myers)
24.	dyclonine hydrochloride	0.05 to 0.1% solution or suspension, 1 to 3 mg. as lozenge	oral anesthetic	May 25, 1982	Sucrets Maximum Strength (SmithKline)
25.	dexbrompheniramine maleate (NDA)	6 mg./12 hours (oral timed-release)	antihistamine	September 3, 1982	Drixoral (Schering)
26.	pseudoephedrine sulfate (NDA)	120 mg./12 hours (oral timed-release)	nasal decongestant	September 3, 1982	Afrinol Repetabs (Schering)
27.	triprolidine hydrochloride	2.5 mg./4-6 hours	antihistamine	November 26, 1982	Actifed Capsules (Warner-Lambert), Actidil Syrup and Capsules (Warner-Lambert)

+FDA approval for OTC marketing is on an interim basis pending adoption of a Final Monograph.

INGREDIENT	ADULT DOSAGE	PRODUCT CATEGORY	DATE OF OTC APPROVAL	PRODUCT EXAMPLES
28. tioconazole (NDA)	1% cream	antifungal	February 18, 1983	TZ-3 (Pfizer)
29. ibuprofen (NDA)	200 mg./4-6 hours (oral)	internal analgesic/ antipyretic	May 18, 1984	Advil (Whitehall), Nuprin (Bristol-Myers)
30. dexbrompheniramine maleate	2 mg./4-6 hours (oral)	antihistamine	January 15, 1985	
31. diphenhydramine hydrochloride	25-50 mg./4-6 hours (oral)	antihistamine	January 15, 1985	Benadryl 25 (Warner-Lambert)
32. pseudoephedrine hydrochloride(NDA)	120 mg./12 hours (oral timed-release)	nasal decongestant	June 17, 1985	Actifed (Warner-Lambert)
33. triprolidine hydrochloride (NDA)	5 mg./12 hours	antihistamine	June 17, 1985	Actifed 12-hour Capsules (Warner-Lambert)
34. oxymetazoline hydrochloride (NDA)	0.025% solution/drops (topical)	occular vasoconstrictor	May 30, 1986	Ocuclear (Schering)
35. pyrantel pamoate	11 mg./kilo of body weight maximum dose 1 gram (oral)	anthelmintic	August 1, 1986	Antiminth (Pfizer)
36. povidone iodine sponge (NDA)	10% (new dosage form)	antimicrobial	January 7, 1987	E-Z Scrub 241 (Deseret)
37. diphenhydramine hydrochloride	25-50 mg./4-6 hours (oral)	antiemetic	April 30, 1987	
38. dexbrompheniramine maleate (NDA)	3 mg./6-8 hours (oral)	antihistamine	May 22, 1987	Drixoral Plus (Schering)
39. chlophedianol hydrochloride	25 mg./6-8 hours (oral)	antitussive	August 12, 1987	
40. doxylamine succinate	7.5 mg. - 12.5 mg./4-6 hours (oral)	antihistamine	August 24, 1987	Nyquil (Procter & Gamble)
41. loperamide (NDA)	4 mg., then 2 mg., 8 mg./day (oral)	antidiarrheal	March 3, 1988	Imodium A-D (Johnson & Johnson)
42. hydrogenated soybean oil and lecithin	12.4 gm. powder in 2-3 oz. water 20 minutes before gall bladder x-rays	cholecystokinetic	February 28, 1989	Liposperse (Merck)
43. clotrimazole (NDA)	1% lotion and cream/2 times daily	antifungal	October 23, 1989	Lotrimin AF (Schering)
44. permethrin (NDA)	1% cream rinse	pediculicide (head lice)	May 5, 1990	Nix (Warner-Lambert)
45. clotrimazole (NDA)	1% cream & 100 mg inserts	anticandidal	November 30, 1990	Gyne-Lotrimin (Schering), Mycelex-7 (Miles)
46. miconazole nitrate	2.0% cream and 100 mg. inserts	anticandidal	March 13, 1991	Monistat 7 (Ortho)
47. hydrocortisone	above 0.50% to 1.0%	antipruritic (anti-itch)	August 30, 1991 +	
48. hydrocortisone acetate	above 0.50% to 1.0%	antipruritic (anti-itch)	August 30, 1991 +	
49. clemastine fumarate (NDA)	1.34 mg./12 hours	antihistamine	August 21, 1992	Tavist-1 (Sandoz Consumer)
50. clemastine fumarate (in combination with phenylpropanolamine HCl (NDA)	1.34 mg./12 hours	antihistamine/ decongestant	August 21, 1992	Tavist-D (Sandoz Consumer)
51. dexchlorpheniramine maleate	2 mg/4-6 hours (oral)	antihistamine	December 9, 1992	
52. naproxen sodium (NDA)	200 mg/4-6 hours (oral)	internal analgesic/ antipyretic	January 11, 1994	Aleve (Procter & Gamble)
53. pheniramine maleate with naphazoline HCl (NDA)	0.3%; 0.025% in solution	ophthalmic antihistamine/ decongestant	June 8, 1994	Naphcon A (Alcon), Opcon A (Bausch & Lomb) Ocuhist (Akorn)
54. antazoline phosphate with naphazoline HCl (NDA)	0.5%; 0.05% in solution	ophthalmic antihistamine/ decongestant	July 11, 1994	Vasocon A (Ciba)
55. famotidine (NDA)	10 mg, up to 20 mg/day	acid reducer	April 28, 1995	Pepcid AC (J&J•Merck)
56. ibuprofen suspension 100mg/5ml for pediatric use (NDA)	7.5 mg/kg up to 4 times a day	internal analgesic antipyretic	June 16, 1995	Children's Motrin (McNeil Consumer)

	INGREDIENT	ADULT DOSAGE	PRODUCT CATEGORY	DATE OF OTC APPROVAL	PRODUCT EXAMPLES
57.	cimetidine (NDA)	200 mg up to twice per day	acid reducer	June 19, 1995	Tagamet HB (SmithKline)
58.	ketoprofen (NDA)	12.5 mg every 4 to 6 hours	Internal analgesic	October 16, 1995	Orudis KT (Whitehall-Robins), Actron (Bayer)
59.	ranitidine (NDA)	75 mg up to twice per day	acid reducer	December 19, 1995	Zantac 75 (Warner Wellcome)
60.	butoconazole nitrate (NDA)	2.0% cream and applicators (3 days)	anticandidal	December 26, 1995	Femstat 3 (Procter & Gamble)
61.	minoxidil (NDA)	2.0% topical solution	hair grower	February 9, 1996	Rogaine (Pharmacia & Upjohn)
62.	nicotine polacrilex (NDA)	2 mg and 4 mg gum	smoking cessation	February 9, 1996	Nicorette (SmithKline Beecham)
63.	nizatidine (NDA)	75 mg up to twice daily	acid reducer	May 9, 1996	AXID AR (Whitehall-Robins Healthcare)
64.	miconazole nitrate (NDA)	2.0% cream and 200 mg. inserts	anticandidal	April 16, 1996	Monistat 3 (Ortho)
65.	nicotine transdermal system (NDA)	15 mg. patch	smoking cessation	July 3, 1996	Nicotrol (McNeil Consumer)
66.	clotrimazole (NDA)*	1% cream & 200 mg. inserts	anticandidal	July 29, 1996	Gyne-Lotrimin 3 (Schering-Plough)
67.	nicotine transdermal system (NDA)	21, 14, & 7 mg. patch	smoking cessation	August 2, 1996	Nicoderm CQ (SmithKline Beecham)
68.	bentoquatam (NDA)*	5% lotion	poison ivy protection	August 26, 1996	Ivy Block (EnviroDerm)
69.	cromolyn sodium (NDA)	4% nasal solution	allergy prevention & treatment	January 6, 1997	Nasalcrom (McNeil Consumer)
70.	tioconazole (NDA)	6.5% vaginal ointment	anticandidal	February 11, 1997	Vagistat-1 (Bristol-Myers Squibb), Monistat 1 (McNeil)
71.	loperamide/simethicone (NDA)*	2 mg loperamide, 125 mg simethicone	antidiarrheal/antigas	June 26, 1997	Imodium Advanced (McNeil Consumer)
72.	triclosan (dentifrice) (NDA)*	0.30% triclosan/0.243% fluoride	antigingivitis	July 11, 1997	Total (Colgate-Palmolive)
73.	ketoconazole (NDA)	1% shampoo	dandruff shampoo	October 10, 1997	Nizoral (Johnson & Johnson Consumer Products)
74.	minoxidil (NDA)*	5.0% topical solution	hair grower	November 17, 1997	Rogaine Extra Strength for Men (Pharmacia & Upjohn)
75.	aspirin 250mg/caffiene 65mg/acetaminophen 250mg (NDA)**		migraine	January 14, 1998	Excedrin Migraine
76.	ranitidine (NDA)*	75 mg (effervescent system)	acid reducer	February 26, 1998	Zantac 75 EFFERdose (Glaxo Wellcome)
77.	miconazole nitrate (NDA)*	4.0% cream	anticandidal	March 30, 1998	Monistat 3 (Advanced Care Products)
78.	terbinafine hydrochloride	1.0% cream	antifungal	March 9, 1999	Lamisil AT (Novartis)

+FDA approval for OTC marketing is on an interim basis pending adoption of a Final Monograph. ** New OTC NDA - Not previously Rx* ***New OTC indication*

II. Other Potential OTC Ingredients/Dosages

Note: CHPA Listing of Potential Switches is Based on Published Sources or Publicly Available Information

	INGREDIENT	ADULT DOSAGE	PRODUCT CATEGORY	SOURCE OR INTERIM FDA POSITION, IF KNOWN
1.	acamprosate	-------	alcoholism treatment	Mentioned as hopefully "eventually" an OTC in New York Times, July 31, 1998
2.	acyclovir	200 mg	antiviral	Adv. Cmte. voted "No" on 1/12/95 for OTC management of recurrent genital herpes
3.	albuterol sulfate	2 mg	bronchodilator	Mentioned as switch candidate in *Med Ad News*, Dec., 1996
4.	astemizole	--------	anithistamine	Mentioned as "future switch" in *Switch Newsletter* Feb., 1996
5.	azithromycin	--------	antibiotic	Mentioned as switch candidate in *Med Ad News*, Dec., 1996
6.	beclomethasone dipropionate	nasal spray 0.042%	allergy prevention & treatment	Scheduled Adv. Cmte. consideration on Sept. 19, 1997 - postponed

	INGREDIENT	ADULT DOSAGE	PRODUCT CATEGORY	SOURCE OR INTERIM FDA POSITION, IF KNOWN
7.	butenafine	--------	antifungal	Mentioned as switch candidate in *Drug Store News*, Sept. 7, 1998
8.	cetirizine Hcl	--------	antihistamine	Mentioned as switch candidate in *Drug Topics*, Apr. 6, 1998
9.	cholestyramine	--------	cholesterol-lowering agent	FDA tentative position: cholesterol-lowering agents not appropriate for OTC use.
10.	clotrimazole/betamethasone	--------	antifungal	Mentioned as switch candidate in *Drug Store News*, Sept. 7, 1998
11.	colestipol hydrochloride	-------	cholesterol-lowering agent	FDA tentative position: cholesterol-lowering agents not appropriate for OTC use.
12.	cyclobenzaprine Hcl		muscle spasm treatment	Mentioned as switch candidate in *Med Ad News*, Dec., 1996
13.	diclofenac	topical	non-steroidal anti-inflammatory	Mentioned as switch candidate in *"The Tan Sheet,"* March 23, 1998
14.	diflunisal		non-steroidal anti-inflammatory	*FDC Reports*, November 7, 1988, p.10
15.	econazole nitrate	1%	antifungal	NDA pending, *Progressive Grocer*, April, 1995
16.	erythromycin		antibiotic	*FDC Reports*, June 12, 1989; "Potential switch product" in *Med Ad News*, August, 1996
17.	etodolac	200 mg	non-steroidal anti-inflammatory	*FDC Reports - "The Tan Sheet,"* Sept. 30, 1996, p. 15
18.	fexofenadine		antihistamine	Mentioned as switch candidate in *"The Tan Sheet,"* August 18, 1997
19.	fluconazole		antifungal	Mentioned as "future switch" in *Switch Newsletter* Feb., 1996
20.	fluvastatin	-------	cholesterol-lowering agent	FDA tentative position: cholesterol-lowering agents not appropriate for OTC use.
21.	ibuprofen extended release	-------	non-steroidal anti-inflammatory	
22.	loratadine		antihistamine	Mentioned as "future switch" in *Switch Newsletter* Feb., 1996
23.	lovastatin	--------	cholesterol-lowering agent	FDA tentative position: cholesterol-lowering agents not appropriate for OTC use.
24.	methacarbamol	--------	muscle relaxant	Muscle relaxants discussed by Adv. Cmte. 3/28/95. Issue of switch unresolved
25.	mupirocin	--------	topical antiviral	"Potential switch product" in *Med Ad News*, August, 1996
26.	nabumetone	--------	non-steroidal anti-inflammatory	"Potential switch product" in *Med Ad News*, August, 1996
27.	nicotine	nasal spray, oral inhaler	smoking cessation	"Near-term switch candidates" in *"The Tan Sheet,"* May 19, 1997
28.	nitrofurantoin monohydrate		urinary tract antibiotic	"Potential switch candidate" in *"The Tan Sheet,"* Dec. 16, 1996, p. 7
29.	nystatin		antifungal	Mentioned as switch candidate in *Med Ad News*, Dec., 1996
30.	omeprazole		antisecretory (heartburn)	Procter & Gamble press release, December 15, 1997.
31.	penciclovir		topical antiviral (cold sores)	Narrowly rejected by Adv. Cmte. December 1, 1998
32.	piroxicam		non-steroidal anti-inflammatory	Mentioned as "future switch" in *Switch Newsletter* Feb., 1996
33.	sucralfate		anti-ulcer	NDA pending, *FDC Reports*, January 16, 1989, p. 8.
34.	sulindac	300 mg./day	analgesic	*FDC Reports*, April 3, 1989, p. 7.
35.	theophylline		bronchodilator	Mentioned as switch candidate in *Med Ad News*, Dec., 1996
36.	tretinoin		acne treatment	Mentioned as switch candidate in *OTC News*, June, 1997
37.	valacyclovir	500 mg	antiviral	Mentioned as switch candidate in *"The Tan Sheet,"* August 18, 1997
38.	zanamivir	inhalant	influenza treatment, prophylaxis	Mentioned as switch candidate in *"The Tan Sheet,"* May 12, 1997, p. 15